

In re Application of:  
Rheins and Morhenn  
Application No.: 09/375,609  
Filed: August, 17, 1999  
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PATENT  
Attorney Docket No.: DERM1100-1

### **EXHIBIT B**

#### **CLAIMS AS THEY WILL STAND UPON ENTRY OF THE AMENDMENT**

64. (Amended) A non-invasive method for obtaining a skin sample for use in isolating or detecting a nucleic acid in the skin sample, the method comprising:

(a) applying at least one application of an adhesive to the skin and removing the adhesive from the skin in a manner such that the skin nucleic acid profile after application is not affected for up to about two hours and such that a sample comprising a nucleic acid adheres to the adhesive after its removal, or, scraping the skin with an instrument to remove a sample comprising a nucleic acid from the skin, thereby obtaining a skin sample comprising a nucleic acid; and

(b) isolating or detecting the nucleic acid from the skin sample of step (a).

65. (Amended) The method of claim 64, wherein the skin sample comprises at least one of stratum corneum cells, stratum lucidum cells, stratum granulosum cells, stratum spinosum cells, and stratum basalis cells, or any combination thereof.

70. (Amended) The method of claim 64, wherein the skin sample is isolated by applying the adhesive surface to the skin between one and twenty five times to obtain the skin sample.

71. (Amended) The method of claim 64, wherein the skin sample is isolated by applying the adhesive surface to the skin between one and two times to obtain the skin sample.

72. (Amended) The method of claim 64, wherein the sample is isolated by one application of an adhesive surface to an outer layer of the skin.

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73. The method of claim 64, wherein the adhesive surface comprises an adhesive tape.

74. The method of claim 73, wherein the adhesive tape comprises a duct tape, a Scotch™ tape or a D-SQUAME™ tape.

75. The method of claim 64, wherein a skin sample is isolated by scraping an outer layer of skin with a rigid instrument.

76. The method of claim 64, wherein the nucleic acid comprises a DNA.

77. The method of claim 64, wherein the nucleic acid comprises an RNA.

78. The method of claim 77, wherein the RNA comprises an mRNA.

79. The method of claim 78, wherein the nucleic acid encodes a polypeptide.

80. The method of claim 79, wherein the polypeptide comprises a cytokine.

81. The method of claim 79, wherein the polypeptide comprises an interleukin.

82. (Twice amended) The method of claim 80, wherein the cytokine comprises interleukin-1 (IL-1), interleukin-2 (IL-2), interleukin-3 (IL-3), interleukin-4 (IL-4), interleukin-5 (IL-5), interleukin-6 (IL-6), interleukin-8 (IL-8), interleukin-10 (IL-10), interleukin-12 (IL-12), interleukin-13 (IL-13), granulocyte macrophage colony stimulating factor (GM-CSF), or an interferon, or any combination thereof.

83. The method of claim 78, wherein the polypeptide comprises an inflammatory mediator.

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84. The method of claim 83, wherein the inflammatory mediator comprises a leukotriene or a prostaglandin.

85. The method of claim 64, further comprising identifying or quantifying the nucleic acid.

86. The method of claim 85, wherein identifying or quantifying the nucleic acid is by a polymerase chain reaction (PCR).

87. The method of claim 85, wherein identifying or quantifying the nucleic acid is by hybridization with a polynucleotide probe.

88. The method of claim 85, wherein identifying or quantifying the nucleic acid is by RNase protection assay.

89. The method of claim 85, wherein by identifying or quantifying a nucleic acid in a recovered sample the presence of a local or systemic disease, a disorder, a genetic disease, or an inflammatory reaction is identified, distinguished, or diagnosed.

90. The method of claim 64, wherein the nucleic acid is associated with a local biological reaction.

91. The method of claim 64, wherein the nucleic acid is associated with a systemic biological reaction.

92. (Amended) The method of claim 64, further comprising applying the sample to a DNA array.

93. The method of claim 64, wherein the skin sample is a human skin sample.

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94. (Amended) The method of claim 64, further comprising applying the cellular material sample to a DNA array.

95. A non-invasive method for isolating a nucleic acid in a skin cell of a subject comprising:

- (a) removing an outer skin layer to expose an inner skin layer by scraping or stripping by use of an adhesive;
- (b) removing an inner skin sample from the exposed skin by scraping or stripping by use of an adhesive; and,
- (c) isolating or detecting a nucleic acid sample from the inner skin sample.

97. (Amended) The method of claim 95, wherein the adhesive comprises an adhesive tape.

98. The method of claim 95, wherein the nucleic acid comprises a DNA.

99. The method of claim 95, wherein the nucleic acid comprises an RNA.

100. The method of claim 99, wherein the nucleic acid encodes a polypeptide.

101. The method of claim 95, further comprising identifying or quantifying the nucleic acid.

102. (Amended) The method of claim 95, further comprising applying the nucleic acid, or complementary equivalent, to a DNA array.

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103. The method of claim 95, wherein the skin sample is a human skin sample.

104. (Amended) A non-invasive method for obtaining a skin sample for use in isolating or detecting nucleic acid encoding a cytokine in the skin sample, the method comprising:

applying an adhesive surface to the skin and removing the adhesive surface from the skin such that a skin sample comprising nucleic acid in an amount sufficient for subsequent isolation or detection adheres to the adhesive surface after its removal and in a manner such that the skin nucleic acid profile after application is not affected for up to about two hours, thereby obtaining a skin sample for use in isolating or detecting a nucleic acid in a skin sample.

105. (Amended) The method of claim 104, wherein the skin sample comprises at least one of stratum corneum cells, stratum lucidum cells, stratum granulosum cells, stratum spinosum cells, and stratum basalis cells, or any combination thereof.

106. (Amended) The method of claim 105, wherein the sample is isolated by one application of an adhesive surface to an outer layer of the skin.

111. (Amended) The method of claim 104, wherein the skin sample is isolated by applying an adhesive surface to the skin between one and twenty five times.

112. (Amended) The method of claim 104, wherein the the skin sample is isolated by applying an adhesive surface to the skin between one and two times.

113. The method of claim 104, wherein the adhesive surface comprises an adhesive tape.

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114. The method of claim 113, wherein the adhesive tape comprises a duct tape, a Scotch™ tape or a D-SQUAME™ tape.

115. The method of claim 104, wherein the skin sample is isolated by scraping an outer layer of skin with a rigid instrument.

116. The method of claim 104, wherein the nucleic acid is DNA.

117. The method of claim 104, wherein the nucleic acid is RNA.

118. The method of claim 117, wherein the RNA is mRNA.

119. The method of claim 104, wherein the nucleic acid is a combination of DNA and RNA.

120. (Amended) The method of claim 104, wherein the nucleic acid encodes a polypeptide.

121. The method of claim 120, wherein the polypeptide is a cytokine.

122. The method of claim 120, wherein the polypeptide is an interleukin.

123. (Amended) The method of claim 121, wherein the cytokine is interleukin-1 (IL-1), interleukin-2 (IL-2), interleukin-3 (IL-3), interleukin-4 (IL-4), interleukin-5 (IL-5), interleukin-6 (IL-6), interleukin-8 (IL-8), interleukin-10 (IL-10), interleukin-12 (IL-12), interleukin-13 (IL-13), granulocyte macrophage colony stimulating factor (GM-CSF), or an interferon or any combination thereof.

124. (Amended) The method of claim 121, wherein the cytokine is an inflammatory mediator.

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125. The method of claim 124, wherein the inflammatory mediator is a leukotriene or a prostaglandin.

126. The method of claim 104, wherein the nucleic acid is present in a local biological reaction.

127. The method of claim 104, wherein the nucleic acid is present in a systemic biological reaction.

128. (Amended) The method of claim 104, further comprising applying the sample to a DNA array.

129. The method of claim 104, wherein the skin sample is a human skin sample.

130. The method of claim 104, further comprising isolating or detecting one or more nucleic acids in the skin sample.

131. The method of claim 130, wherein the one or more nucleic acids are amplified by a polymerase chain reaction (PCR) following or during isolation.

132. The method of claim 130, wherein isolating or detecting one or more nucleic acids is by hybridization with a polynucleotide probe.

133. The method of claim 130, wherein isolating or detecting one or more nucleic acids is by RNase protection assay.

134. (Amended) The method of claim 130, further comprising applying the nucleic acid to a DNA array.

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135. (Amended) A non-invasive method for obtaining a skin sample for use in isolating or detecting nucleic acid in the skin sample, the method comprising:

scraping the skin with an instrument to remove a skin sample comprising nucleic acid in an amount sufficient for subsequent isolation or detection, and in a manner such that the skin nucleic acid profile after application is not affected for up to about two hours, thereby obtaining a skin sample for use in isolating or detecting a nucleic acid in a skin sample.

136. (Amended) A non-invasive method for obtaining a skin sample for use in isolating or detecting a nucleic acid in a skin sample, the method comprising:

- (a) scraping the skin with an instrument to remove a sample comprising a nucleic acid from the skin, and in a manner such that the skin nucleic acid profile after application is not affected for up to about two hours, thereby obtaining a skin sample comprising a nucleic acid;
- (b) isolating or detecting the nucleic acid from the skin sample of step (a).

137. The method of claim 80, wherein the cytokine is IL-1.

138. The method of claim 80, wherein the cytokine is IL-2.

139. The method of claim 80, wherein the cytokine is IL-3.

140. The method of claim 80, wherein the cytokine is IL-4.

141. The method of claim 80, wherein the cytokine is IL-5.



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142. The method of claim 80, wherein the cytokine is IL-6.
143. The method of claim 80, wherein the cytokine is IL-8.
144. The method of claim 80, wherein the cytokine is IL-10.
145. The method of claim 80, wherein the cytokine is IL-12.
146. The method of claim 80, wherein the cytokine is IL-13.
147. The method of claim 80, wherein the cytokine is GM-CSF.
148. The method of claim 80, wherein the cytokine is an interferon.
149. A non-invasive method for determining an expression profile in a skin sample, the method comprising:
  - (a) applying at least one application of an adhesive to a sample site on the skin and removing the adhesive from the skin in a manner such that the skin nucleic acid profile after application is not affected for up to about two hours, and such that a sample comprising a ribonucleic acid (RNA) adheres to the adhesive after its removal, or, scraping the skin with an instrument to remove a sample comprising RNA from the skin, thereby obtaining a skin sample comprising RNA; and
  - (b) isolating or detecting RNA from the skin sample of step (a) for determining the expression profile in the skin sample.

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150. The method of claim 149, wherein the skin sample is isolated by applying the adhesive surface to the sample site of the skin between one and twenty five times to obtain the skin sample.

151. The method of claim 149, wherein the RNA is mRNA.

152. The method of claim 149, wherein steps a) and b) are performed repeatedly over time to identify changes in the expression pattern.

153. The method of claim 149, wherein the RNA isolated or detected comprises RNA encoding a cytokine.

154. The method of claim 149, wherein RNA is detected by probing RNA of the sample with a polynucleotide complementary to a sequence of interest.

155. The method of claim 149, wherein RNA is detected using a DNA array.